

**DISSERTATION ON
A STUDY ON THE GASTRO INTESTINAL INVOLVEMENT IN
NEWLY DIAGNOSED HIV PATIENTS**

***Submitted in partial fulfillment of
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**THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
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CERTIFICATE

This is to certify that dissertation entitled “**A STUDY ON THE GASTRO INTESTINAL INVOLVEMENT IN NEWLY DIAGNOSED HIV PATIENTS**” is a bonafide work done by **DR.A.SANGEETHA**, post graduate student, Institute of Internal Medicine, Madras Medical College, Chennai - 3 in partial fulfillment of the University Rules and Regulations for the award of MD Branch - I General Medicine, under our guidance and supervision, during the Academic period from March 2008 to April 2011.

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ABBREVIATIONS

AFB	- Acid – fast bacilli
AIDS	- Acquired immunodeficiency syndrome
ART	- Antiretroviral therapy
CD4	- Human T helper cells expressing CD4 antigen (T helper cell)
CDC	- Centers for Disease Control and Prevention (USA)
CMV	- Cytomegalovirus
CNS	- Central nervous system
CRAG	- Cryptococcal antigen
CSF	- Cerebrospinal fluid
CT	- Computed tomography
CXR	- Chest X-ray
DNA	- Deoxyribonucleic acid
HIV	- Human immunodeficiency virus
HSV	- Herpes simplex virus
IRS	- Immune restoration syndrome
JC	- Jacob Creutzfeldt (Virus)
LGE	- Linear gingival erythema
MOT	- Mycobacteria other than tuberculosis

P24 - A soluble antigen produced by HIV

PCR - Polymerase chain reaction

PGL - Persistent generalized lymphadenopathy

PLWHA - People living with HIV / AIDS

PML - Progressive multifocal leukoencephalopathy

RF - Rectal fistula

RVF - Rectovaginal fistula

RNA - Ribonucleic acid

TB - Tuberculosis

TLC - Total lymphocyte count

WHO - World Health Organization

ZN - Ziehl-Neelsen (staining method)

HAART - Highly Active Anti Retroviral Therapy

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INTRODUCTION

INTRODUCTION⁶²

Diseases of the gastrointestinal tract are common among those who are HIV – infected. Sometimes the first clue that a previously undiagnosed patient is HIV-infected is the presence of a HIV-associated gastrointestinal condition. These conditions can lead to significant morbidity including pain, difficulty in swallowing, diarrhea, and weight loss. Early diagnosis and treatment can substantially improve the lives of those who are afflicted by these conditions. Although identifying the specific etiology of a patient's symptoms can be challenging, a methodical approach can usually identify a treatable condition.

ORAL LESIONS:

The most common HIV-associated oral condition is candidiasis, or thrush. Thrush is usually found in those with advanced immunodeficiency, generally in patients with a CD4+ T cell count less than 300 cells/mm³. Oral candidiasis is associated with progression to AIDS, and the presence of thrush in someone who is not known to be HIV infected should prompt a recommendation for HIV testing.

Oral hairy leukoplakia (OHL): Thought to be due to Epstein-Barr virus, the lesions are asymptomatic and are generally of only cosmetic importance. OHL sometimes responds to acyclovir or valacyclovir, although probably the best treatment is HAART induced immune reconstitution. As with thrush, OHL is highly predictive of HIV.

Aphthous ulcers are common and often severe in those who are HIV infected.

Oral lesions that do not heal within two weeks or those that are accompanied by systemic signs such as fever should be biopsied to rule out other etiologies such as deep fungal infection or malignancy.

Single shallow painless ulcerations can be due to syphilis (condyloma lata), and should be screened for with a rapid plasma reagin (RPR) test.

Warts can be found on the lips or in the oral cavity and are typically painless. Kaposi's sarcoma (KS) can be found anywhere in the GI tract.

ESOPHAGEAL LESIONS:

Disease involving the esophagus is common in advanced HIV infection, and is most commonly due to Candida. Patients with

candidal esophagitis usually have oropharyngeal involvement as well and present with dysphagia and odynophagia.

In cases of esophagitis that fail to respond to antifungal therapy, endoscopy with biopsy is required to rule out other etiologies such as herpes simplex virus (HSV), cytomegalovirus (CMV), malignancy, or aphthous ulcerations.

DIARRHEA:

World wide, diarrhea is the most common cause of morbidity and mortality among those who are HIV - infected. Diarrhea can be caused by bacterial, viral or parasitic infections, or by a medication.

The evaluation of a patient with diarrhea begins with a thorough history and physical examination.

In patients with advanced immunodeficiency, fever, and anemia, opportunistic infections such as those caused by Mycobacterium avium complex (MAC) and CMV must be considered.

In those who present with symptoms of greater than one-week duration associated with weight loss, fever, dehydration, or bloody stools, diagnostic studies are indicated.

The most common bacterial causes of diarrhea are Salmonella, C. difficile, MAC, shigella, and Campylobacter. The overall incidence of bacterial colitis has been reduced by the widespread use of trimethoprim / sulfamethoxazole (TMP/FMX) for Pneumocystis prophylaxis.

Common parasitic causes of diarrhea include Cryptosporidium, Microsporidium and Entamoeba histolytica.

Diarrhea due to rotavirus or other viral agents is relatively common but is usually self-limited.

In those with advanced immunosuppression (typically CD4 counts of $<50/\text{mm}^3$) CMV can lead to colitis, but since the introduction of HAART, the incidence of active CMV disease has fallen dramatically.

Histoplasmosis can involve the gastrointestinal tract, leading to diarrhea, fever, pain, and weight loss. Diagnosis can be made by the detection of intracellular budding yeast in colonic biopsy specimens. The histoplasmosis urinary antigen is very useful for diagnosing this infection and for monitoring therapy.

ANORECTAL DISEASE:

Both HSV1 and 2 commonly cause anorectal disease. HSV infection can also lead to urinary symptoms, impotence, and sacral paresthesias. In HIV-infected patients who present with perianal ulcerative lesions or fissures, the most common cause is HSV.

Gonorrhea, syphilis, and chlamydia:

Patients who are infected with *Neisseria gonorrhoea* and *Chlamydia trachomatis* can present with symptoms that include anal discharge, pain, tenesmus, and bleeding. Cultures of rectal swabs and urine ligase chain reaction (LCR) for Gonorrhea and Chlamydia infection can be useful in making the diagnosis.

Warts, caused by human papillomaviruses (HPV) are commonly found in the perianal area.



AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

To determine the association between CD4 count and GIT manifestations.

To evaluate the common symptoms and etiology of GIT manifestations.



REVIEW OF LITERATURE

REVIEW OF LITERATURE

WHO Clinical Staging of HIV for Adults and Adolescents with Confirmed HIV Infection⁵⁸ :

The clinical staging and case definition of HIV for resource-constrained settings were developed by the WHO in 1990 and revised in 2007. Staging is based on clinical findings that guide the diagnosis, evaluation and management of HIV/AIDS, and does not require a CD4 cell count. This staging system is used in many countries to determine eligibility for antiviral therapy. Clinical stages are categorized as 1 through 4, progressing from primary HIV infection to advanced HIV / AIDS. These stages are defined by specific clinical conditions or symptoms. For the purpose of the WHO staging system, adolescents and adults are defined as individuals aged ≥ 15 years.

Table : 1

WHO Clinical Staging of established HIV infection

HIV ASSOCIATED SYMPTOMS	WHO CLINICAL STAGE
Asymptomatic	1
Mild Symptoms	2
Advanced Symptoms	3
Severe Symptoms	4

Clinical Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage 2

- Unexplained moderate weight loss (<10% of presumed or measured body weight^a)
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical Stage 3

- Unexplained^b severe weight loss (>10% of presumed or measured body weight)
- Recurrent chronic diarrhea for longer than one month
- Unexplained persistent fever (above 37.5° intermittent or constant, for longer than one month)

- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections(eg,pneumonia,empyema,pyomyositis,bone or joint infection, meningitis,bacteremia)
- Acute necrotizing ulcerative stomatitis,gingivitis or periodontitis
- Unexplained anaemia(<8 gm/dl),neutropenia ($<0.5 \times 10^9$ per liter) and / or chronic thrombocytopaenia ($<50 \times 10^9$ per liter)

Clinical Stage 4 ^c

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)

- Central nervous system toxoplasmosis
 - HIV encephalopathy
 - Extrapulmonary cryptococcosis including meningitis
 - Disseminated non-tuberculous mycobacterial infection
 - Progressive multifocal leukoencephalopathy
 - Chronic cryptosporidiosis
 - Chronic isosporiasis
 - Disseminated mycosis (extrapulmonary histoplasmosis or coccidioidomycosis)
 - Recurrent septicaemia (including non-typhoidal Salmonella)
 - Lymphoma (cerebral or B-cell non – Hodgkin)
 - Invasive cervical carcinoma
 - Atypical disseminated leishmaniasis
 - Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy
- a- Assessment of body weight in pregnant woman needs to consider the expected weight gain of pregnancy
- b- Unexplained refers to where the condition is not explained by other causes.

c- Some additional specific conditions can also be included in regional classifications (such as reactivation of American trypanosomiasis (meningoencephalitis and / or myocarditis) in the WHO Region of the Americas and penicilliosis in Asia).

Table : 2
CRITERIA FOR HIV STAGING EVENTS ⁵⁹
Adults (15 years or older)

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
Asymptomatic.	No HIV – related symptoms reported and no signs on examination.	Not applicable.
Persistent generalized lymphadenopathy.	Painless enlarged lymphnodes > 1 cm in two or more non – contiguous sites (excluding inguinal) in the absence of known cause and persisting for three months or more.	Histology.
Herpes zoster.	Painful vesicular rash in dermatomal distribution of a nerve supply, does not cross the midline.	Clinical diagnosis.

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
Unexplained chronic diarrhea for longer than one month.	Chronic diarrhea (loose or watery stools three or more times daily) reported for longer than one month.	Three or more stools observed and documented as unformed, and two or more stool tests reveal no pathogens.
Unexplained persistent fever (intermittent or constant and lasting for longer than one month).	Fever or night sweats for more than one month, either intermittent or constant with reported lack of response to antibiotics or antimalarial agents, without other obvious foci of disease on examination; malaria must be excluded in malarious area.	Documented fever $>37.5^{\circ}\text{C}$ with negative blood culture, negative Ziehl-Neelsen stain, negative malaria slide, normal or unchanged chest X-ray and no other obvious focus of infection.
Persistent oral candidiasis.	Persistent or recurring creamy white curd-like plaques that can be scraped off (pseudomembranous) or red patches on tongue, palate or lining of mouth, usually painful or tender (erythematous form).	Clinical diagnosis.
Pulmonary tuberculosis	Chronic symptoms: (lasting at least 2-3 weeks) cough,	Isolation of M.Tuberculosis on

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
(current).	haemoptysis, shortness of breath, chest pain, weight loss, fever, night sweats; PLUS EITHER Positive sputum smear; OR Negative sputum smear; AND Compatible chest radiograph (including but not restricted to upper lobe infiltrates, cavitation, pulmonary fibrosis). No evidence of extra pulmonary disease.	sputum culture or histology of lung biopsy (with compatible symptoms).
Severe bacterial infection (such as pneumonia, meningitis, empyema, pyomyositis, bone or joint infection, bacteraemia and severe pelvic inflammatory disease).	Fever accompanied by specific symptoms or signs that localize infection and response to appropriate antibiotic.	Isolation of bacteria from appropriate clinical specimens (usually sterile sites).

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
Pneumocystis pneumonia.	<p>Dyspnoea on exertion or nonproductive cough of recent onset (within the past three months), tachypnoea and fever;</p> <p>AND</p> <p>Chest X-ray evidence of diffuse bilateral interstitial infiltrates;</p> <p>AND</p> <p>No evidence of bacterial pneumonia; bilateral crepitations on auscultation with or without reduced air entry.</p>	Cytology or immunofluorescent microscopy of induced sputum or bronchoalveolar lavage or histology of lung tissue.
Chronic herpes simplex virus infection (orolabial, genital or anorectal) of more than one month or visceral infection of any duration.	Painful, progressive anogenital or orolabial ulceration; lesions caused by recurrence of herpes simplex virus infection and reported for more than one month. History of previous episodes. Visceral herpes simplex virus requires definitive diagnosis.	Positive culture or DNA (by polymerase chain reaction) of herpes simplex virus or compatible cytology or histology.
Oesophageal candidiasis.	Recent onset of retrosternal pain or difficulty on	Macroscopic appearance at

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
	swallowing (food and fluids) together with oral candidiasis.	endoscopy or bronchoscopy, or by microscopy or histology.
Extrapulmonary tuberculosis.	<p>Systemic illness (such as fever, night sweats, weakness and weight loss). Other evidence for extra pulmonary or disseminated tuberculosis varies by site:</p> <p>Pleural, pericardial, peritoneal involvement, meningitis, mediastinal or abdominal lymphadenopathy or osteitis.</p> <p>Discrete peripheral lymph node Mycobacterium tuberculosis infection (especially cervical) is considered a less severe form of extrapulmonary tuberculosis.</p>	<p>M. tuberculosis isolation or compatible histology from appropriate site or radiological evidence of miliary tuberculosis;</p> <p>(diffuse uniformly distributed small military shadows or micronodules on chest X-ray).</p>
Extrapulmonary cryptococcosis (including meningitis).	Meningitis: usually subacute, fever with increasing severe headache, meningism, confusion, behavioral changes that	Isolation of Cryptococcus neoformans from extrapulmonary site or positive

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
	respond to cryptococcal therapy.	cryptococcal antigen test on cerebrospinal fluid or blood.
Chronic cryptosporidiosis (with diarrhea lasting more than one month).	No presumptive clinical diagnosis.	Cysts identified on modified Ziehl-Neelsen stain microscopic examination of unformed stool.
Symptomatic HIV-associated nephropathy.	No presumptive clinical diagnosis.	Renal biopsy.

Table : 3

WHO immunological classification for established HIV infection⁵⁹

HIV-associated immunodeficiency	>5 years of age (absolute number per mm³ or % CD4+)
None or not significant	> 500
Mild	350 – 499
Advanced	200 – 349
Severe	<200 or <15%

CDC Classification System for HIV Infection⁵⁶ :

The CDC categorization of HIV/AIDS is based on the lowest documented CD4 cell count and on previously diagnosed HIV-related conditions. If a patient had a condition that once met the criteria for Category B but now is asymptomatic, the patient would remain in Category B. Additionally, categorization is based on specific conditions, as indicated below. Patients in categories A3, B3, and C1-C3 are considered to have AIDS.

Table : 4

CDC Classification System for HIV Infection

CD4+ count Categories	Clinical Categories		
	A Asymptomatic, Acute HIV, or PGL	B Symptomatic Conditions, not A or C	C AIDS- Indicator Conditions
(1) ≥ 500 cells/μL	A1	B1	C1
(2) 200-499 cells/μL	A2	B2	C2
(3) < 200 cells/μL	A3	B3	C3

CDC Classification System: Category A

Consists of one or more of the following conditions listed below in an adolescent or adult (>13 years) with documented infection. Conditions listed in categories B and C must not have occurred.

- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy
- Acute (primary) HIV infection with accompanying illness or history of acute HIV infection

CDC Classification System: Category B: Symptomatic Conditions

Category B symptomatic conditions are defined as symptomatic conditions occurring in an HIV-infected adolescent or adult that are not included among conditions listed in clinical category C and that meet at least 1 of the following criteria:

- a) They are attributed to HIV infection or indicate a defect in cell-mediated immunity.
- b) They are considered to have a clinical course or management that is complicated by HIV infection.

Examples include, but are not limited to, the following:

- Bacillary angiomatosis
- Oropharyngeal candidiasis (thrush)
- Vulvovaginal candidiasis, persistent or resistant
- Pelvic inflammatory disease (PID)
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Hairy leukoplakia, oral
- Idiopathic thrombocytopenic purpura
- Constitutional symptoms, such as fever ($>38.5^{\circ}\text{C}$) or diarrhea lasting >1 month
- Peripheral neuropathy
- Herpes zoster (shingles), involving ≥ 2 episodes or ≥ 1 dermatome

CDC Classification System: Category C: AIDS-Indicator Conditions

- Bacterial pneumonia, recurrent (≥ 2 episodes in 12 months)
- Candidiasis of the bronchi, trachea, or lungs

- Candidiasis, esophageal
- Cervical carcinoma, invasive, confirmed by biopsy
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1-month duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcers (>1-month duration), or
bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1-month duration)
- Kaposi sarcoma
- Lymphoma, Burkitt, immunoblastic, or primary central nervous
system
- Mycobacterium avium complex(MAC) or M.kansasii,
disseminated or extrapulmonary
- Mycobacterium tuberculosis , pulmonary or extrapulmonary
- Mycobacterium , other species or unidentified species,

- disseminated or extrapulmonary
- *Pneumocystis jiroveci* (formerly *carinii*) pneumonia (PCP)
- Progressive multifocal leukoencephalopathy (PML)
- *Salmonella* septicemia, recurrent (nontyphoidal)
- Toxoplasmosis of brain
- Wasting syndrome due to HIV (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhea (≥ 2 loose stools per day ≥ 1 month) or chronic weakness and documented fever ≥ 1 month

GIT MANIFESTATIONS⁷⁰ :

Highly active antiretroviral therapy (HAART) has dramatically decreased opportunistic infections (OIs) in human immunodeficiency virus (HIV)-infected patients. However, gastrointestinal disease continues to account for a high proportion of presenting symptoms in these patients. Gastrointestinal symptoms in treated patients who respond to therapy are more likely to be the result of drug-induced complications than OI. Endoscopic evaluation of the gastrointestinal tract remains a cornerstone of diagnosis, especially in patients with advanced immunodeficiency, who are at risk for OI. The peripheral

blood CD4+ lymphocyte count helps to predict the risk of an OI, with the highest risk seen in HIV-infected patients with low CD4 count (<200 cells/mm³).

ORAL THRUSH:

In a systematic literature review ⁶⁵ Candidiasis was the most common (28.6%) GIT manifestation followed by hairy leukoplakia (9.3%), Kaposi sarcoma (2.5%), ulceration (2.5%), herpes simplex (1.2%), papilloma (0.6%), and 4.4% had periodontal disease. Only 1.2% reported xerostomia. There were no differences in the prevalence of oral manifestations of HIV infection between age groups, sexes, modes of transmission and types of drug therapy.

Oropharyngeal candidiasis occurs frequently among HIV-infected individuals, particularly those with more advanced immuno suppression. The diagnosis of oral candidiasis is a CDC category B diagnosis. The presence of oropharyngeal candidiasis is an indication for initiating prophylaxis for *Pneumocystis pneumonia* and for initiating antiretroviral therapy. Although HIV-related immuno suppression is typically the most important risk factor for candidiasis, other factors can contribute, including use of antibiotics that change normal bacterial flora, use of corticosteroids, use of chemotherapeutic drugs, presence of

diabetes, decreased salivary flow rates, and wearing dentures. Considering the strong association of HIV infection and oropharyngeal candidiasis, HIV assessment and testing is recommended for any person who presents with oropharyngeal candidiasis and does not have a known risk factor for oropharyngeal candidiasis.

ESOPHAGUS:

CANDIDA:

Ana Luiza Werneck-Silva, Ivete Bedin Prado et al⁷⁰ reported *Candida* spp. continue to be the most common cause of OI in the esophagus, followed by viral infection, especially CMV. Patients often present with dysphagia, but may also develop odynophagia and/or acute retrosternal chest pain. The presence of oral candidiasis (thrush) suggests candidal esophagitis. On the other hand, the absence of thrush per se does not exclude it. At endoscopy, *Candida* esophagitis shows a characteristic superficial mucosal pattern: focal or confluent yellowish white plaques that overlie an erythematous mucosa. It is seldom related to mucosal ulceration, which in general results from causes other than *Candida* infection. Endoscopy has also been used to grade the severity of *Candida* infection. They analyzed the relationship between *Candida* esophagitis severity and peripheral blood CD4 cell count in a

prospective study of a large cohort of adult HIV-infected patients. They suggest that even in immuno suppressed HIV-infected patients, immunological status may play a role in limiting Candida disease in initial grades, but seems to be irrelevant in the following progression of the infection. Other mechanisms, such as the local epithelial defenses, may be involved with the development of these OIs in the GI mucosa.

DIARRHEA:

In a recent study ⁵⁵ involving 388 homosexual men about 12% of the asymptomatic men were found to have enteric pathogens. Subsequently half of these patients were found to be HIV positive. 60% of the symptomatic men had enteric infections, and about 65% of them were HIV positive; this establishes a strong association between gut infection and HIV seropositivity. Of the AIDS patients who were asymptomatic from a gastrointestinal viewpoint 40% had evidence of enteric infection.

In a recent study ⁶⁶ in Britain 107 consecutive patients who either had AIDS or were HIV positive were referred to a gastrointestinal service for assessment of persistent diarrhea. This group represented fewer than 10% of the HIV-positive patients followed up at that institution. Six stool samples were obtained from each of the study

patients for bacteriologic assessment. Sigmoidoscopy and colonoscopy were performed as well. Of the 71 AIDS patients 26 had *Cryptosporidium* infection. An infectious cause of the diarrhea could not be found in only 6 of the 71 patients.

The authors concluded that there was little need to implicate noninfectious causes of diarrhea in AIDS patients. In contrast, only one-third of the HIV-positive patients without AIDS had an identifiable enteric cause for their diarrhea. Perhaps the enteropathy of HIV infection is an early manifestation that assumes less importance as the disease progresses and the host becomes more susceptible to enteric pathogens.

In the study ⁶⁷ of 143 HIV/AIDS adult patients with diarrhea, a total of 23 cases with *Cryptosporidium* infection and 120 with *Cryptosporidium* negative were reported during the study period. The prevalence of cryptosporidiosis was 16.1%. The factors associated with *Cryptosporidium* infection were female gender, history of diarrhea >21 days, low CD4+count and WBC count < 4,000 cells/ mm³. There was a strong association between cryptosporidiosis and CD4+count.

Blanshard et al⁶⁸ have studied the course of the infection in 128 patients and identified four clinical patterns of disease: transient (28.7 per cent), chronic (59.7 per cent), fulminant (7.8 per cent) and asymptomatic (3.9 per cent). Transient disease occurred in patients with a wide range of CD4 lymphocyte counts, but was more common in less immuno suppressed patients. Fulminant disease, defined by the passage of more than 21 stools / day from the time of presentation, only occurred in patients with a CD4 count of less than $50/\text{mm}^3$. This group had lost more than 7 kg in weight at presentation and more commonly had other intercurrent gastrointestinal infections. They survived for a median of only 5 weeks, compared with 20 weeks for those with chronic diarrhoea and 36 weeks for those with transient infection. The survival was unaffected by any treatment other than zidovudine.

ANORECTAL DISEASES:

Anal and perianal manifestations are frequent during HIV infection, especially in homosexual patients. Some lesions are related to general diseases, some others to immuno suppression. Anal herpetic lesions are most frequently noted. Proctological examination with microbiological and histological studies mostly offers an accurate diagnosis.

LIVER DISEASE⁶⁹:

Liver disease due to chronic hepatitis B and C is currently one of the leading causes of morbidity and mortality among HIV-positive patients in the developed world. Non coinfecting patients with chronic hepatitis C tend to progress to end-stage liver disease in 20-30 years, whereas coinfecting patients have higher rates of progression. ESLD is common in coinfecting patients. The prevalence of HCV and/or HBV coinfection is high in developed countries. Studies⁶⁹ performed in European HIV-positive patients showed rates of 33% and 9%, respectively while in the USA figures are very similar, 28% and 9%. **Martínez et al⁶⁹** in Spain analysed the cause of 235 deaths in 4471 patients (5%) on combination antiretroviral therapy (cART) from 1997 until 2004. The number of patients who died from ESLD increased from 8% in 1997 to 41% in 2004, and in recent years this condition has become the leading cause of death in HIV-positive patients.

Rosenthal et al⁶⁹ in France determined mortality due to ESLD in a nationwide population of HIV-positive patients. The authors followed a total of 20,940 HIV-positive patients, 4005 (19.9%) of whom were coinfecting, and showed mortality due to ESLD represented 23.7% of non-AIDS-related deaths. In this population 92.6% of patients who

died from ESLD had chronic HCV infection. A prospective, observational study⁶⁹ of 11 cohorts carried out in Europe, the United States and Australia included 23,441 HIV-1–infected patients (22.5% were HCV-positive) and followed them from December 1999 until February 2004. This study showed that, of the 1246 deaths recorded, those related to AIDS were the most frequent (31.1%), while liver disease was the most frequent non–AIDS-related cause (14.5%). HCV infection was shown to be an independent predictor of liver-related death .

SPLENIC INVOLVEMENT IN TB IN HIV PATIENTS:

In a systematic literature review **Ramakant Dixit et al**⁶³ reported the splenic involvement in tuberculosis seems to be more frequent in patients with HIV infection and in disseminated form of disease. Ultrasonography of the spleen is simple, easily available, affordable, non-invasive, imaging technique highly useful for the diagnosis of splenic involvement in tuberculosis. The sonographic findings should be correlated with overall clinical presentation with demonstration of tuberculosis at other body sites and image guided FNAC may be considered in cases with isolates splenic involvement.

Most of the patients (62%) were in the age group of 26-50 years. The males were three times more commonly affected than females. 75% of the patients had fever as a presenting symptom followed by anorexia and weight loss in 50% cases. Pain abdomen was the major abdominal symptom seen in 62% cases followed by abdominal distension in 12% cases. Among co-morbid illness, HIV infection was seen in 50% cases.

On Sonography, splenic lesion commonly presents as multiple regular hypo-echoic nodule representing tuberculoma and sometimes irregular hypo-echoic lesion representing splenic abscess, especially in the presence of HIV infection. Similar sonographic pattern is also being reported in AIDS related lymphomatous involvement of spleen.

MATERIALS AND METHODS

MATERIALS & METHODS

Study Design:

Observational study

Study Population:

HIV positive patients attending ART centre, Medical OPD, GGH, Chennai.

Inclusion Criteria:

HIV positive patients

Exclusion Criteria:

> 60 years

Diabetic patients

On steroid therapy

Known malignancy

Organ transplant

On Chemotherapy

Ethical Clearance:

Obtained

Informed Consent:

Obtained from all patients

Methodology:

A total of 65 patients were identified over a period of 12 months according to the above criteria and were included in the study. Of there only 40 patients turned up for follow up and participated in the study.

A questionnaire prepared noted the age, sex, address, primary complaints, GIT symptoms, medical illness such as SHT, psychiatric disorders, substances abuse, smoking, alcoholism and other complaints if any.

Clinical examination included a detailed examination from head to foot, examination of cardiac, respiratory, GIT and nervous system.

Perianal, per rectal, per vaginal examination (in females) was done.

Laboratory Investigations:

The following investigations are done in all patients during their **first visit:**

Blood sugar, urea, creatinine

Liver function test

Complete blood count

HBsAg

Anti HCV

CD4 count

CXR, sputum AFB

USG abdomen and pelvis

During subsequent visit:

1. Stool for ova, cyst, occult blood and stool culture
2. OGD scopy

If needed basis,

CT abdomen and pelvis plain and contrast

Ascitic fluid analysis including AFB culture

Pleural fluid analysis including AFB culture

Sputum AFB stain

Lumbar puncture and CSF analysis including AFB culture, India

ink preparation for Cryptococcus

Nerve Conduction Study

MRI Brain with MRA & MRV

Tzanck smear

Table : 5

Parameters

S.No.	Parameter	Method
1.	Complete blood count	Automated flow cytometry
2.	ESR	Westergren method
3.	Urea	GLDH/urease
4.	Creatinine	Picrate method
5.	Serum albumin	Bromocresol green
6.	Serum bilirubin	Calorimetric endpoint diazo
7.	Total Protein	Biuret method
8.	Stool for parasites	Conc method (sat. saline floatation) & iodine, modified ZN stain
9.	Occult blood in stools	Standard guaiac test
10.	HBsAg	Rapid detection kit
11.	Anti HCV	ELISA
12.	CD4+ count	Fluorescence Activated cell Sorter (FACS)

Statistical Analysis:

Data analysis was done with use of SPSS, version 13. Descriptive statistics were used to calculate the frequency, mean, and standard deviation. To examine the linear trend of the proportions, trend chi-square was used and to find the test of association chi-square was computed.

Financial support:

Nil

Conflicts of interest:

None

Table : 6
Normal Values

Hemoglobin	M: 13.3 – 16.2 gms%	F: 12.0 – 15.8gms%
PCV	M:38.8 – 46.4	35.4 – 44.4
Total Count	3.54 – 9.06 x 10 ³ /mm ³	
Platelet Count	165 – 415 x 10 ³ /mm ³	
MCV	80 – 100 fL	
MCHC	32.3 – 35.9g/dL	
MCH	26.7 – 31.9 pg/cell	
ESR	M:0 – 15mm/hr	F:0-20mm/hr
Reticulocyte count	M:0.8 – 2.3%	F:0.8 – 2.0%
Creatinine	M:0.6 – 1.2mg/dl	F:0.5 – 0.9mg/dl
BUN	7 – 20 mgs/dl	
Total Bilirubin	0.3 – 1.3 mgs/dl	
Direct Bilirubin	0.1 – 0.4 mgs/dl	
SGOT	12 – 38 U/L	
SGPT	7 – 41 U/L	
Se.Alkaline phosphatase	33 – 96 U/L	
Total Protein	6.7 – 8.6 gms/dl	
Se.Albumin	3.5 – 5.5 gms/dl	
HBsAg	Negative	
Anti HCV	Negative	
CD 4+ count	500 – 1500 cells per mm ³	



OBSERVATION AND RESULTS

OBSERVATION & RESULTS

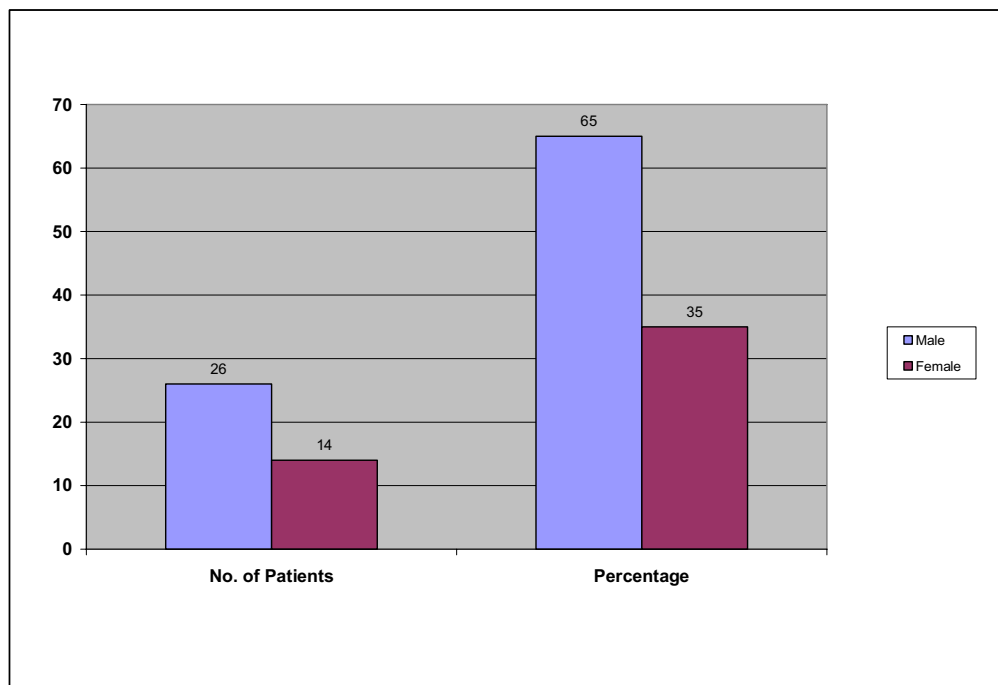
STUDY POPULATION CHARACTERISTICS:

TABLE : 7

SEX DISTRIBUTION

SEX	NO. OF PATIENTS	PERCENTAGE	P value
Male	26	65%	0.058
Female	14	35%	

FIGURE : 1 SEX-WISE DISTRIBUTION OF PATIENTS

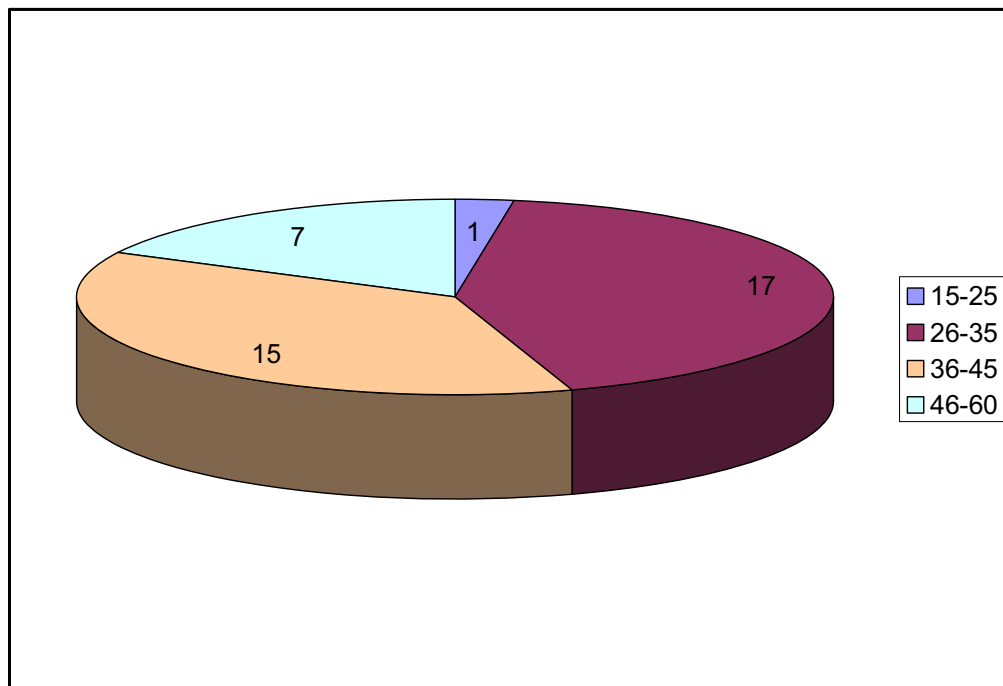


In our study, 26 (65%) patients were male, and 14 (35%) patients were female, though it is not statistically significant with a P value of 0.058.

TABLE : 8
AGE DISTRIBUTION

AGE GROUP	NO. OF PATIENTS	MALE	FEMALE	PERCENTAGE
15 - 25	1	0	1	2.5%
26 – 35	17	11	6	42.5%
36 – 45	15	10	5	37.5%
46 – 60	7	5	2	17.5%

FIGURE : 2 AGE WISE DISTRIBUTION OF PATIENTS

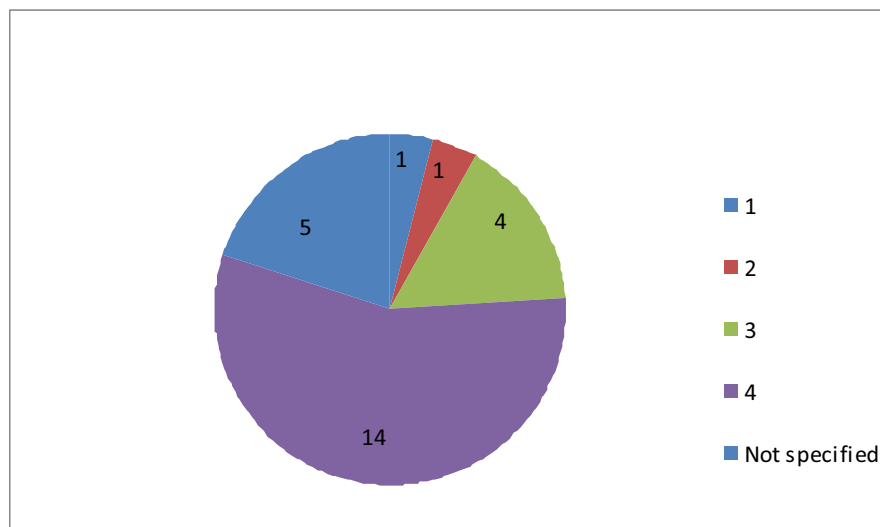


Among 40 patients in our study 32(80%) were in the age group of 26 to 45 years, which is statistically significant with a P value of 0.001 The Mean Age of the patients included in the study was 42.55 mean years, with S.D. of 3.178 years.

TABLE : 9
WHO CLINICAL STAGING

STAGE	NO. OF PATIENTS	MALE	FEMALE	PERCENTAGE
1	1	0	1	4%
2	1	0	1	4%
3	4	1	3	12%
4	14	12	2	56%
Not specified	5	4	1	20%

FIGURE : 3 WHO CLINICAL STAGING

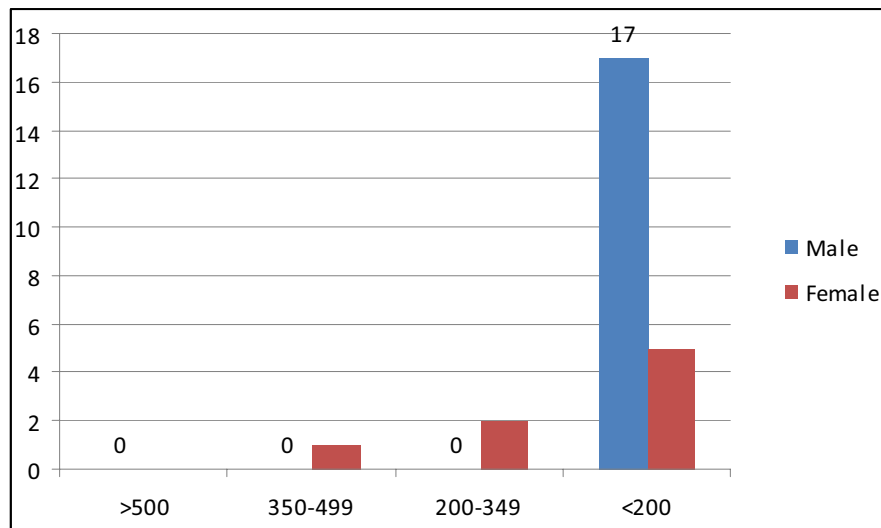


Among 25 new patients in our study 12 (48%) male patients were in WHO stage 4 which is statistically significant with a P value of 0.04. 4 (16%) of patients were in WHO stage 3. 5(20%) of patients not met the WHO clinical staging criteria of HIV.

TABLE : 10
WHO IMMUNOLOGICAL CLASSIFICATION

CD 4+ COUNT	MALE	FEMALE	PERCENTAGE
>500	0	0	0%
350-499	0	1	4%
200-349	0	2	8%
<200	17	5	88%

FIGURE : 4 WHO IMMUNOLOGICAL CLASSIFICATION

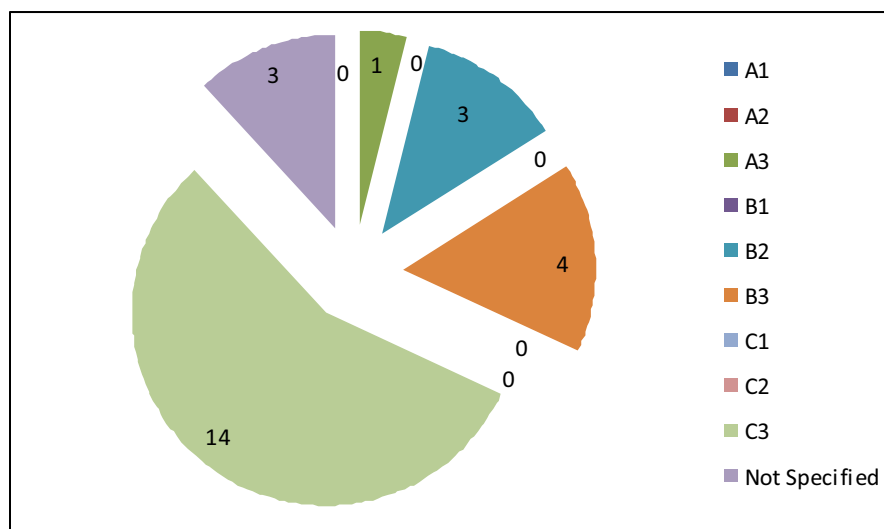


Among 25 new patients in our study 2(8%) patients were in advanced immunosuppression when presented for the first time for HIV diagnosis, 22(88%) patients were in severe immunosuppression, which is statistically significant with a P value of 0.027.

TABLE : 11
CDC CLASSIFICATION

CDC	MALE	FEMALE	PERCENTAGE
A1	0	0	0%
A2	0	0	0%
A3	0	1	4%
B1	0	0	0%
B2	0	3	12%
B3	2	2	16%
C1	0	0	0%
C2	0	0	0%
C3	12	2	56%
Not specified	3	0	12%

FIGURE : 5 CDC CLASSIFICATION



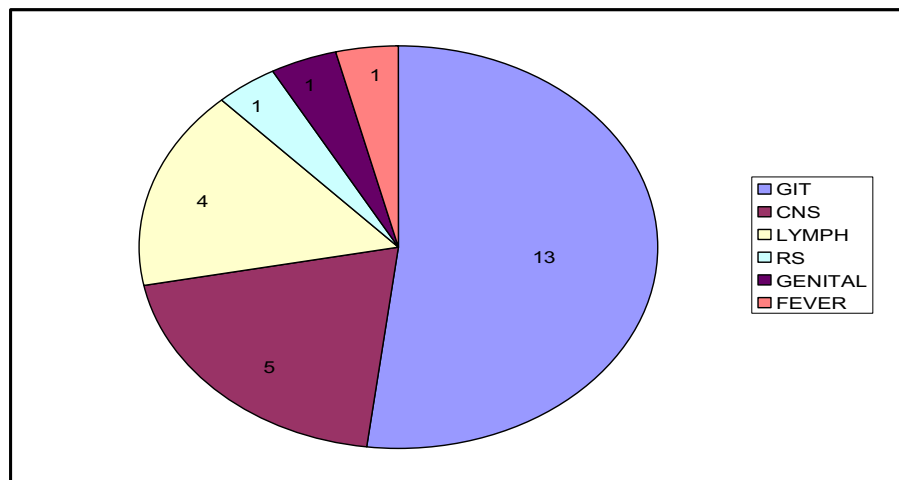
In our study 14(56%) patients were belong to CDC classification C3 at the time of diagnosis, which is statistically significant with a P value of 0.014

TABLE : 12

SYSTEM INVOLVED AT THE TIME OF DIAGNOSIS

SYSTEM	NO. OF PATIENTS	PERCENTAGE
GIT	13	52%
CNS	5	20%
LYMPH	4	16%
RS	1	4%
GENITAL	1	4%
FEVER	1	4%

**FIGURE : 6 SYSTEM INVOLVED AT THE TIME OF
DIAGNOSIS**

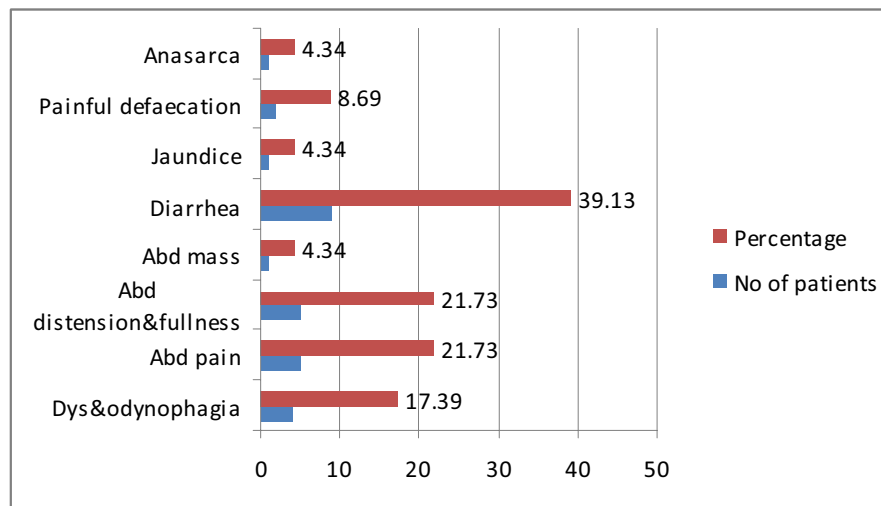


In our study GIT (52%) is the most common system involved at the time of diagnosis of HIV infection, which is statistically significant with a P value of 0.001 followed by central nervous system and lymphatic system.

TABLE : 13
GIT SYMPTOMATOLOGY

SYMPTOM	NO. OF PATIENTS	PERCENTAGE
Dys & odynophagia	4	17.39%
Abdominal pain	5	29.73%
Abdominal distension & fullness	5	29.73%
Abdominal mass	1	4.36%
Diarrhea	9	31.93%
Jaundice	1	4.36%
Painful defecation	2	8.69%
Anasarca	1	4.36%

FIGURE : 7 GIT SYMPTOMATOLOGY

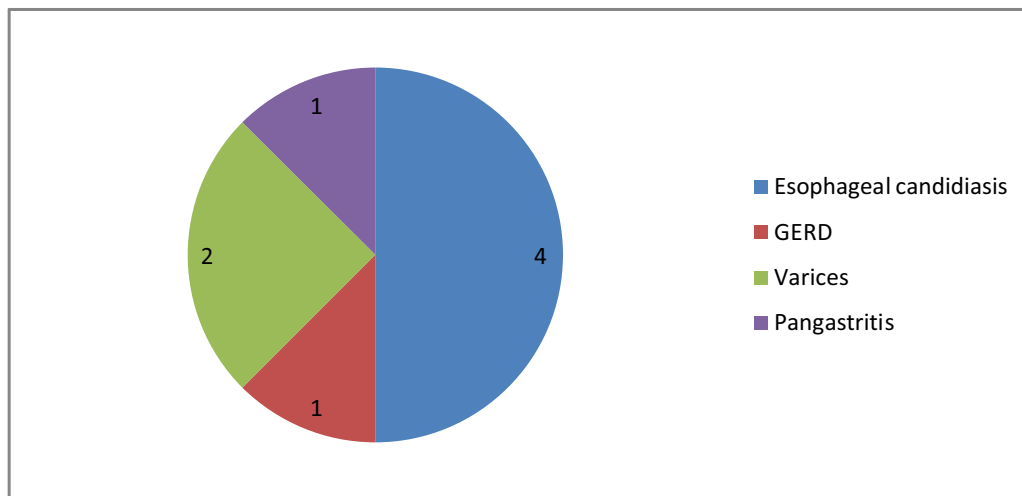


In our study diarrhea (31.93%) is the most common GIT symptom, which is statistically significant with a P value of 0.025, followed by abdominal pain, fullness, distension & dysphagia, odynophagia.

TABLE : 14
ENDOSCOPY FINDINGS

FINDING	NO. OF PATIENTS	PERCENTAGE
Esophageal candidiasis	4	50%
GERD	1	12.5%
Esophageal varices	2	25%
Pan gastritis	1	12.5%

FIGURE : 8 ENDOSCOPY FINDINGS

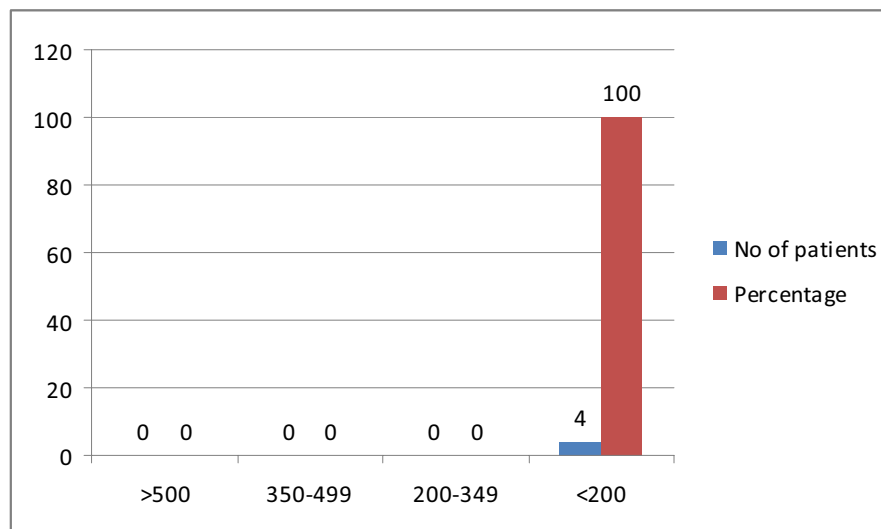


In 8 patients underwent UGI endoscopy 4 (50%) patients had esophageal candidiasis followed by esophageal varices in 2 (25%) patients.

TABLE : 15
ESOPHAGEAL CANDIDIASIS & CD4+COUNT

CD4+COUNT	NO. OF PATIENTS	PERCENTAGE
>500	0	0%
350-499	0	0%
200-349	0	0%
<200	4	100%

FIGURE : 9 ESOPHAGEAL CANDIDIASIS AND CD4+COUNT

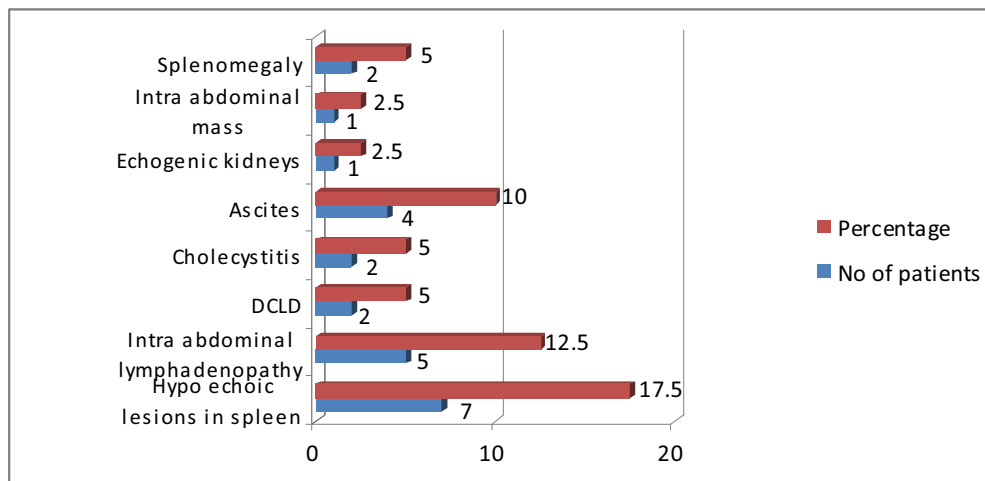


In our study all patients with esophageal candidiasis had CD4+count <200 cells / mm³ which is statistically significant with a P value of <0.001.

TABLE : 16
USG FINDINGS

FINDING	NO. OF PATIENTS	PERCENTAGE
Hypo echoic lesions spleen	7	17.5%
Intra abdominal lymph adenopathy	5	12.5%
DCLD	2	5%
Cholecystitis	2	5%
Ascites	4	10%
Echogenic kidneys	1	2.5%
Intra abdominal mass	1	2.5%
Splenomegaly	2	5%

FIGURE : 10 USG FINDINGS

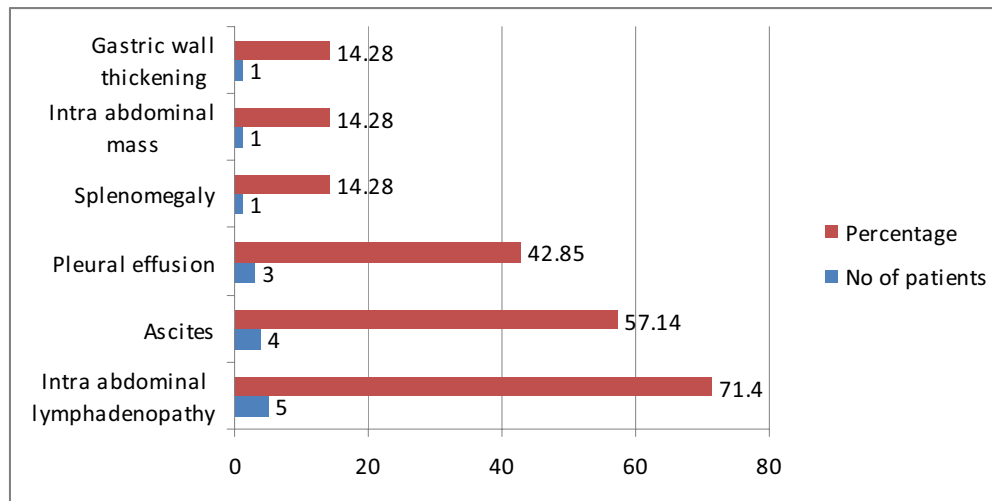


In our study hypoechoic lesions in spleen was seen in 7(17.5%) patients, though it is not statistically significant with a P value of 0.154 which is followed by intra abdominal lymphadenopathy & ascites each in 5 (12.5%) patients.

TABLE : 17
HYPOECHOIC LESIONS IN SPLEEN

ASS FINDING	NO. OF PATIENTS	PERCENTAGE
Intra abdominal lymphadenopathy	5	71.4%
Ascites	4	57.14%
Pleural effusion	3	42.85%
Splenomegaly	1	14.28
Intra abdominal mass	1	14.28
Gastric wall thickening	1	14.28

FIGURE : 11 HYPOECHOIC LESIONS IN SPLEEN



Intra abdominal lymphadenopathy(71.4%) is the common associated finding in patients with hypoechoic lesions in spleen, which is not statistically significant with a P value of 0.287 followed by ascites & pleural effusion.

TABLE : 18

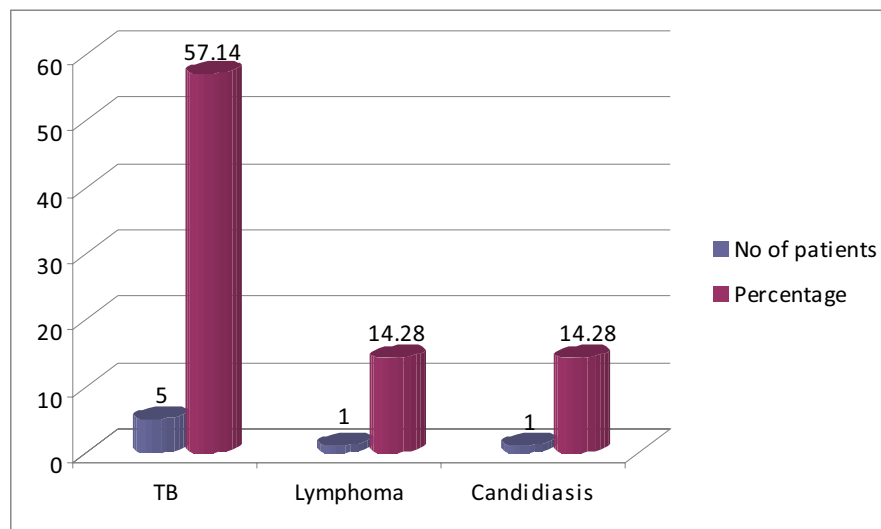
ASSOCIATED DISEASES & HYPOECHOIC

LESIONS IN SPLEEN

DIAGNOSIS	NO. OF PATIENTS	PERCENTAGE
TB	5	57.14%
Lymphoma	1	14.28%
Candidiasis	1	14.28%

FIGURE : 12 ASSOCIATED DISEASES & HYPOECHOIC

LESIONS IN SPLEEN

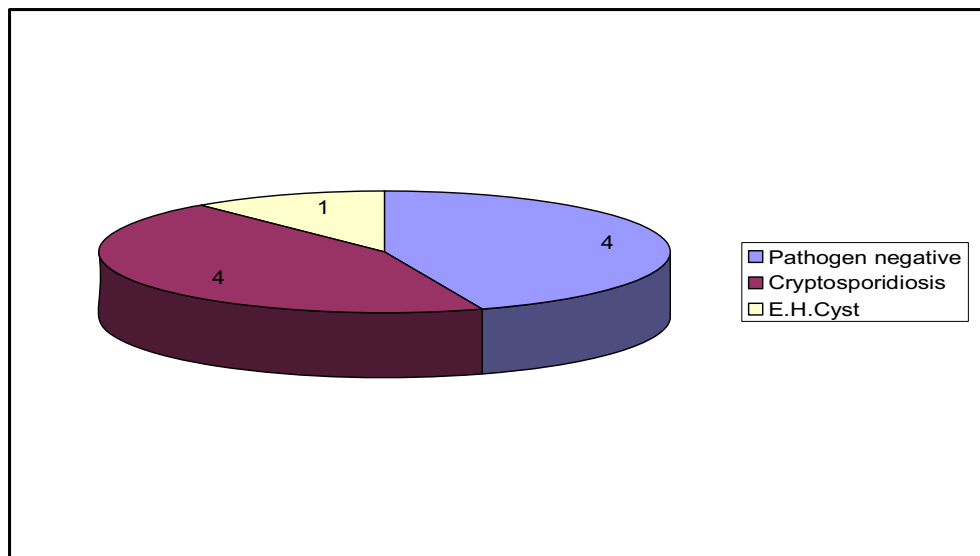


In our study TB is the most common associated disease in patients with spleen hypoechoic lesions which is not statistically significant with a P value of 0.102.

TABLE : 19
CAUSES OF DIARRHEA

DIAGNOSIS	NO. OF PATIENTS	PERCENTAGE
Pathogen negative	4	44.44%
Cryptosporidiosis	4	44.44%
E.H cyst	1	11.11%

FIGURE : 13 CAUSES OF DIARRHEA

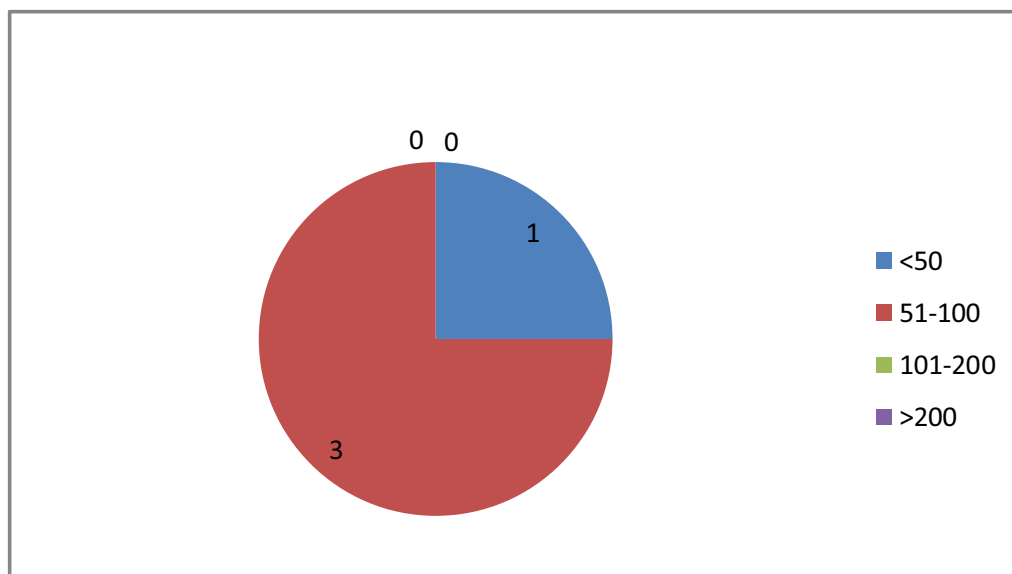


In our study pathogen negative diarrhea & cryptosporidiosis contributed to 8(88.88%) cases of diarrhea, which is not statistically significant with a P value of 0.368.

TABLE : 20
CRYPTOSPORIDIOSIS & CD4+COUNT

CD4+COUNT	NO. OF PATIENTS	PERCENTAGE
<50	1	25%
51-100	3	75%
101-200	0	0%
>200	0	0%

FIGURE : 14 CRYPTOSPORIDIOSIS & CD4+COUNT



In our study all cases of cryptosporidiosis had CD4+count <100, which is not statistically significant with a P value of 0.317

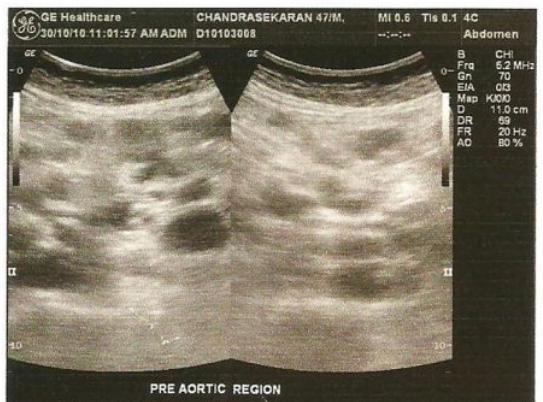
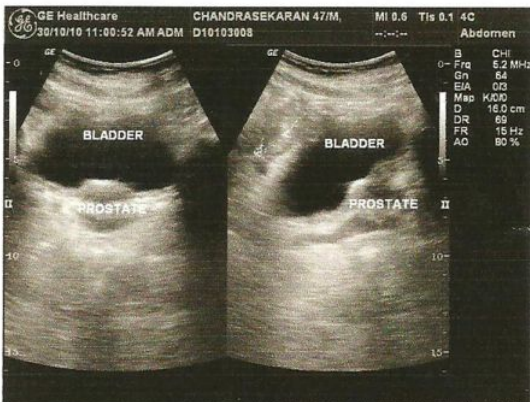
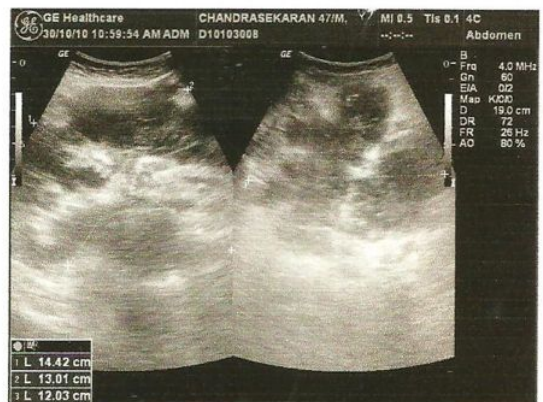
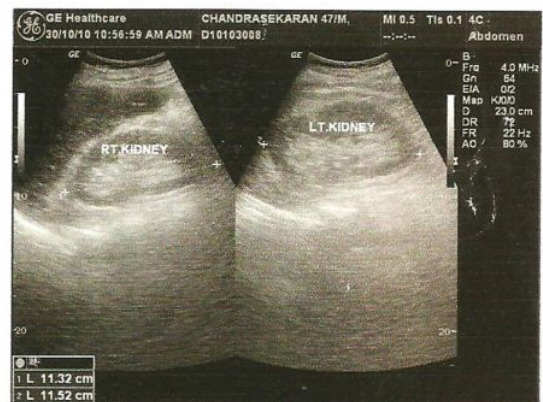
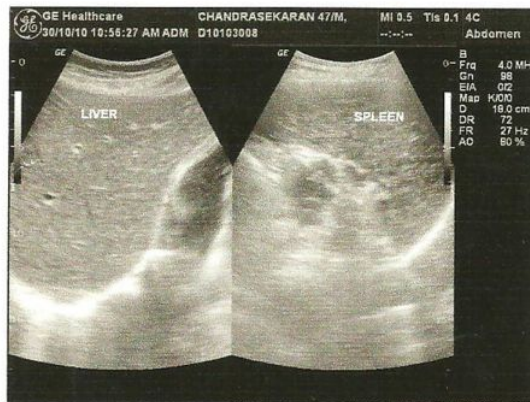


Fig: 15 USG Abdomen and Pelvis showing few tiny calculi in the GB with features of chronic cholecystitis/ a lobulated inhomogenously hypoechoic lesion 14.4/13/12cm in size with ill defined margins in the right lower abdomen with pre and paraaortic lymphadenopathy/ multiple hypoechoic lesions in spleen.

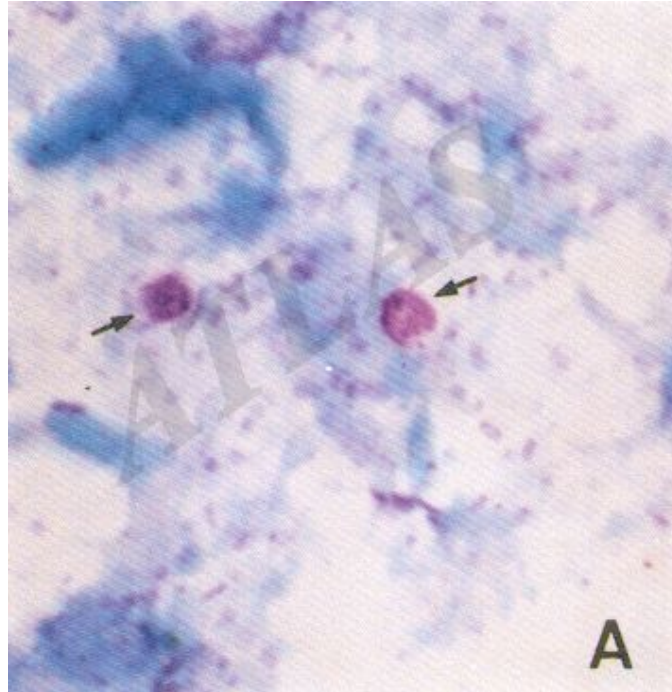


Fig: 16 Oocyst of *Cryptosporidium parvum* on AFB strain in stool analysis.

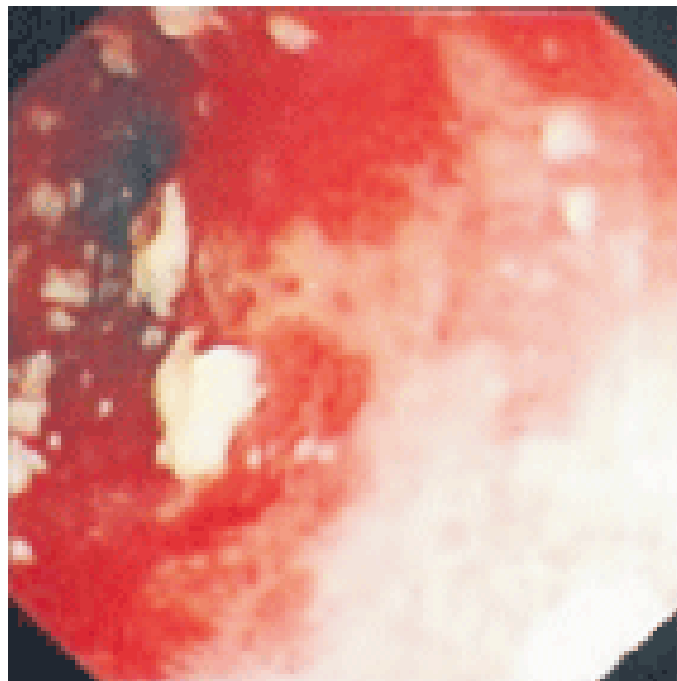


Fig: 17 Esophageal candidiasis in OGD scopy.

DISCUSSION

DISCUSSION

CHARACTERISTICS OF STUDY POPULATION:

Most of our patients in the study group were males (65%). Females contributed to 35% of patients. Most of our patients in the study group were in the age group of 26 to 35 years (42.5%) and immediately followed by patients in the age group of 36 to 45 years (37.5%).

56% of patients in our study group were in WHO Clinical Stage 4 at the time of diagnosis. 20% of patients had clinical disease not represented in WHO Clinical Stages. The diseases are decompensated chronic liver disease, acute inflammatory demyelinating polyneuropathy, cerebrovascular accident.

88% of patients in our study group were in severe immunodeficiency in WHO immunological classification at the time of diagnosis. 56% of patients in our study group were in CDC Classification System C3 at the time of diagnosis. Similar to WHO Clinical Staging system 12% of patients were not represented in this classification also. The diseases are decompensated chronic liver disease, cerebrovascular accident.

GASTRO INTESTINAL INVOLVEMENT :

Gastrointestinal symptoms contributed to the diagnosis of HIV infection / AIDS in 52% of our cases followed by central nervous system in 20%, lymphatic system in 16%. Unexplained fever, respiratory system, genital system each contributed to 4%.

In our study 57.5% of patients had gastro intestinal symptoms. In that diarrhea is the most common (39.13%) symptom, followed by abdominal pain, fullness, distension (29.73%) & dysphagia, odynophagia (17.39%). Both nausea and vomiting were excluded.

Similar results were observed in a study done by **Joseph Bick et al**⁶². He reported that worldwide diarrhea is the most common cause of morbidity and mortality in those who are HIV infected.

In our study endoscopy done for 8 patients who had major UGI symptoms. All patients with the history of dysphagia and odynophagia had esophageal candidiasis. All the cases were associated with oral thrush. Similar results were observed in the following study. **Ana Luiza Werneck-Silva, Ivete Bedin Prado et al**⁷⁰ reported *Candida* spp. continue to be the most common cause of OI in the esophagus, followed by viral infection, especially CMV. Presence of oral thrush

suggests esophageal candidiasis. On the other hand, the absence of thrush per se does not exclude it.

STOOL ANALYSIS:

In patients with diarrhea, cryptosporidiosis and pathogen negative diarrhea contributed to 44.44% of cases each. 11.11% of cases had amoebiasis.

In a recent study⁶⁶ in Britain 107 consecutive patients who either had AIDS or were HIV positive were referred to a gastrointestinal service for assessment of persistent diarrhea. This group represented fewer than 10% of the HIV-positive patients followed up at that institution. Six stool samples were obtained from each of the study patients for bacteriologic assessment. Sigmoidoscopy and colonoscopy were performed as well. Of the 71 AIDS patients 26 had *Cryptosporidium* infection. An infectious cause of diarrhea could not be found in only 6 of the 71 patients.

The authors concluded that there was little need to implicate noninfectious causes of diarrhea in AIDS patients. In contrast, only one-third of the HIV-positive patients without AIDS had an identifiable enteric cause for their diarrhea. Perhaps the enteropathy of HIV infection is an early manifestation that assumes less importance as the

disease progresses and the host becomes more susceptible to enteric pathogens.

USG ABDOMEN&PELVIS:

In our study 17.5% patients had hypo echoic lesions in spleen and was the common abnormality in USG followed by intra abdominal lymphadenopathy in 12.5% of patients. In those who had hypo echoic lesions in spleen intra abdominal lymphadenopathy was the most common associated finding followed by ascites and pleural effusion. TB was the most common associated diseases in patients with spleen hypo echoic lesions. Non Hodgkins lymphoma and candidiasis were the other diseases. On follow up one of the five patients with tuberculosis had expired due to liver failure.

Similar results were observed in a study done by **Ramakant Dixit et al** ⁶³ . They observed 50% of the patients of TB involving spleen were HIV patients.

In our study 2 (8.69%) patients had liver involvement in the form of decompensated chronic liver disease. One patient had coexistent HCV infection. He was a I.V. drug abuser. Another patient had coexistent alcohol abuse with percutaneous exposure to shaving instrument.

LIMITATIONS OF THE STUDY

- The major limitation of our study is small number of subjects we have included in our study.
- Colonoscopy was not done in our patients. So substantial number of structural causes of diarrhea missed in our study.
- Spleen hypo echoic lesions were not aspirated and microbiological tissue diagnosis was not made. This is one of the major limitation of the study.

CONCLUSION

CONCLUSION

- HIV infection more commonly seen in males (65%) when compared to females(35%).
- HIV infection is diagnosed most commonly in the age group 26-45 years.
- At the time of diagnosis 56% of patients are in WHO Clinical Stage 4. 88% of patients are in WHO Immunological Classification Severe immuno suppression. 56% of patients are in CDC Classification System C3. Cerebro vascular disease and decompensated chronic liver disease are not represented in WHO Clinical and CDC Classification System. AIDP also not represented in WHO Clinical Staging.
- GIT is the most common (52%) system involved at the time of diagnosis of HIV infection followed by central nervous system and lymphatic system.
- Diarrhea is the most common (31.93%) GIT symptom followed by abdominal pain, fullness, distension & dysphagia, odynophagia.

- All patients with esophageal candidiasis had CD4+count <200 cells/mm³. All of them had oral thrush.
- In USG hypoechoic lesions in spleen is the most common abnormality followed by intra abdominal lymphadenopathy & ascites.
- In HIV patients TB is the most common associated disease in patients with hypoechoic lesions in spleen.
- Pathogen negative diarrhea & cryptosporidiosis are the common (88.88%) causes of diarrhea. All cases of cryptosporidiosis had CD4+count <100 cells/mm³
- Hence this study concludes that sometimes the first clue that a previously undiagnosed patient is HIV-infected is the presence of an HIV-associated gastrointestinal condition. So it is mandatory to investigate for HIV/AIDS routinely in all patients admitted for GIT complaints.

AREAS OF FUTURE RESEARCH

More efficient programs for early diagnosis of HIV to prevent transmission are urgently required.

Spleen involvement in HIV patients needs extensive research regarding etiology, response to treatment with ATT in patients having associated tuberculosis, antifungal therapy in patients having associated candidiasis, its impact on overall prognosis of these patients.



BIBLIOGRAPHY

BIBLIOGRAPHY

1. Joint United Nations programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO) (2009) AIDS epidemic update 2009: pdf: “UNAIDS/09.36E/ JC1700E”. Accessed 11th October 2010.
2. United Nations Programme on HIV/AIDS (UNAIDS) (2007) Report on the global HIV/AIDS epidemic. Sub-Saharan Africa AIDS epidemic update Regional Summary 2007. Geneva: Joint United Nations Programme on HIV/AIDS. Page 18. Accessed 1 March 2010.
3. Alikor DE, Erhabor NO (2006) Trend of HIV-seropositivity among children in a tertiary health institution in the Niger Delta Region of Nigeria. *Afr J Health Sci* 13: 80-5.
4. Raufa A (2000) Rising HIV infection through blood transfusion worries Nigerian health experts. *AIDS Ann Afr* 11:15.
5. Udonwa NE, Ekpo M, Ekanem IA, Inem VA, Etokidem A (2004) Oil doom and AIDS boom in the Niger Delta Region of Nigeria. *Rural Remote Health* 4: 273:12.

6. Lawn SD (2004) AIDS in Africa: the impact of coinfection on the pathogenesis of HIV – infection. *J Infect Dis* 48: 1-12.
7. Gallo RC (2002) Human retroviruses after 20 years: a perspective from the past and prospects for their future control. *Immunol Rev* 185: 236-65.
8. Federal Ministry of Health (FMOH) – Abuja (2001) Guidelines for the use of antiretroviral (ARV) drugs in Nigeria.
9. Weidle P, Mastro T, Grant A, Nkengasong J, Macharia D (2002) HIV / AIDS treatment and HIV vaccines for Africa. *The Lancet* 359: 2261 – 2267.
10. Federal Ministry of Health (FMOH) – Abuja (2004) Guidelines for the use of antiretroviral (ARV) drugs in Nigeria.
11. Forbi JC and Agwale SM (2009) Inverted CD4+/CD8+ratio associated with AIDS event and death in HIV – type 1 infected individual at first entry in an African nation. *Tan J Health Res* 11: 144 – 148.
12. Centers for Disease Control and Prevention (1992) 1993 revised classification system for HIV infection and expanded

surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep 41: 1- 19.

13. Volberding P (1992) Clinical spectrum of HIV disease. In Devita T, Hellman S, Rosenberg SA, eds. AIDS: Etiology, Diagnosis, Treatment and Prevention, 3rd edn. Philadelphia: Lippincott. 123-40.
14. Schneider MF, Gange SJ, Williams CM (2005) Patterns of the hazard of death after AIDS through the evolution of antiretroviral therapy: 1984 – 2004. AIDS 19: 2009 – 18.
15. World Health Organization, UNAIDS, UNICEF (2008) Towards Universal access: Scaling up priority HIV/AIDS interventions in the health sector: progress report: Geneva: World Health Organization.
16. Lamptey PR (2002) Reducing heterosexual transmission of HIV in poor countries. BMJ 324: 207 – 11.
17. WHO (2005) Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance, African region.

18. Chama CM, Morrupa JY, Abja UA, Kayode A (2009) Normal CD4 T-lymphocyte baseline in healthy HIV-negative pregnant women. J Obstet Gynaecol 29:702-4.
19. Saag MS (1994) Natural History of HIV disease. In Broder S, Merigan TC Jr, Bolognesi D. Text Book of AIDS Medicine, Baltimore. Williams & Wilkin 45- 53.
20. CD4 Collaborative Group (1992) Use of monitored CD4 cell counts: predictions of the AIDS epidemic in Scotland. AIDS 6:213-22.
21. Porter K, Wall PG, Evans BG (1993) Factors associated with lack of awareness of HIV infection before diagnosis of AIDS. BMJ 307: 20-3.
22. Valdiserri RO (2007) Late HIV diagnosis: Bad medicine and worse public health Plos. Med 4: e.200.
23. Marks G, Crepaz N, Janssen RS (2006) Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA AIDS 20: 1447- 1450.
24. Mkanta WN, Mejia MC, Duncan RP (2010) Race, outpatient mental health service use, and survival after an AIDS diagnosis

in the highly active antiretroviral therapy era. *AIDS parent Care STDS* 24:31-7.

25. Delmas MC, Jadad C, De Vincenzi I, Deveau C, Persoz A, Sobel A, Kazatchkine M, Brunet JB, Meyer L (1997) Gender difference in CD4+ cell counts persist after HIV-1 infection. SEROCO Study Group. *AIDS* 11: 1071.3.
26. Camara M, Dieye TN, Seydi M, Diallo AA, Fall M, Diaw PA, Sow PS, Mboup S, Kestens L, Jennes W (2010) Low level CD4+ T cell activation in HIV- exposed seronegative subjects: influence of gender and condom use. *J infect* 201: 835-42.
27. Kitahata, M.M., Gange, S.J., Abraham, A.G., et al. (2009). Effect of early versus deferred antiretroviral therapy for HIV on Survival. *N Eng J Med* 360: 1815 – 1826.
28. Sanders GD, Bayourmi AM, Sundaram V, Bilir SP, Neukermans CP, Rydzak CE, Douglass LR, Lazeroni LC, Holodniy M, Owens DK (2005) Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. *N Eng J Med* 352: 570-585.
29. Dosekun O, Kober C, Richardson D, Parkhouse A, Fisher M, (2010) It's not all swine flu.... are missing opportunities to

diagnose primary HIV infection in patients with flu symptoms?

Int J STD AIDS 21:145-6.

30. Hendriks JC, Satten GA, van Druten HA, Coutinho RA, van Griensven GJ (1998) The incubation period to AIDS in injecting drug users estimated from prevalent cohort data, accounting for death prior to an AIDS diagnosis. AIDS 12: 1537-44.
31. Touloumi G, Karafoulidou A, Gialeraki A, Katsarou O, Milona I, Kapsimali V, Mandalaki T, Hatzakis A (1998) Determinants of progression of HIV infection in a Greek hemophilia cohort followed for up to 16 years after seroconversion. J Acquir Immune Defic Syndr Hum Retrovirol 19: 89-97.
32. Benthem BH, Veugelers PJ, Cornelisse PG, Strathdee SA, Kaldor JM, Shafer KA, Coutinho RA, van Griensven GJ (1998) Is AIDS a floating point between HIV seroconversion and death? Insights from the Tricontinental Seroconverter Study. AIDS 12: 1039-45.
33. Kiwanuka N, Laeyendecker O, Robb M, Kigozi G, Arroyo M, McCutchan F, Eller LA, Eller M, Makumbi F, Birx D, Wabwire-Mangen F, Serwadda D, Sewankambo NK, Quinn TC, Wawer M, Gray R. J Infect Dis. (2008) Effect of human

- immunodeficiency virus Type 1 (HIV-1) subtype on disease progression in persons from Rakai, Uganda, with incident HIV – 1 infection *J. Infect Dis* 197: 638-9.
34. Morgan D and Whitworth J (2001) The natural history of HIV – 1 infection in Africa. *Nat Med* 7: 143 – 5.
 35. Morgan D, Malamba SS, Orem J, Mayanja B, OKongo M, Whitworth JA (2000) Survival by AIDS defining condition in rural Uganda *Sex Transm Infect* 76: 193 -197.
 36. Isingo R, Zaba B, Marston M, Ndege M, Mngara J, Mwita W, Wringe A, Beckles D, Chagalucha J, Urassa M (2007) Survival after HIV infection in the pre-antiretroviral therapy era in rural Tanzanian cohort *AIDS* 6: S5-S13.
 37. Centers for Disease Control and Prevention (2006) Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR* 55 (RR -14) : 1-17.
 38. Sharma SK, Mohan A. Extra pulmonary tuberculosis. *Indian J Med Res* 2004; 120: 316-53.

39. Bastounis E, Pikoulis E, Varelas P, Cirochristos D, Aessopos A. Tuberculoma of the spleen: a rare but important clinical entity. *Am Surg* 1999; 65 131-32.
40. Ozaras R, Celik AD, Zengin K, Mert A, Ozturk KR, Cicek Y, et al. Is laparotomy necessary in the diagnosis of fever of unknown origin? *Acta Chir Belg* 2005; 105: 89-92.
41. Neki NS, Batra KS, Sharma PK, Sidhu BS, Multani LS, Sharma N. Isolated Tubercular Splenic abscess. *J Assoc physicians India* 2001; 49: 759 – 60.
42. Sharma SK, Dun Smith – Rohrberg, Mohammad Tahir, Alladi Mohan, Ashu Seith. Radiological manifestations of splenic tuberculosis: A 23 patient series from India. *Ind J Med Res* 2007; 125: 669-78.
43. Pedro –Botet J. Maristany MT, Miralles R, et al. Splenic tuberculosis in patients with AIDS. *Rev infect Dis* 1991; 13(6): 1069-71.
44. Valencia ME, Moreno V, Soriano V, et al. Hepatic and splenic abscesses formation in patients with tuberculosis (TB) and AIDS.

Int Conf AIDS. 1996, July 7-12; 11: 326 (abstract No. Tu. B. 2354).

45. Sahoo SP, Shukla HS. Abdominal tuberculosis. In: Sharma SK, Mohan A, ed. Tuberculosis, Jaypee brothers, New Delhi, 2001: pg. 187-200.
46. Shah VD, Dixit R, Solanki RN, patel DR, shah PK, Patel SB. Asymptomatic splenic involvement in tuberculosis. Curr Med Trends 2003; 7: 1461-3.
47. HoPL, Chim CS, Yuen KY. Isolated splenic tuberculosis presenting with pyrexia of unkown origin. Scand J Infect Dis 2000; 32(6) : 700 – 01.
48. Prathmesh CS, Tamhankar AP, Rege SA, Shah SR. Splenic tuberculosis and HIV -1 infection. Lancet 2002; 369 (26) 353.
49. Jain M, Singh S, Thomas S, Jain D. Acid –fast bacilli positive isolated tubercular splenic abscess in a HIV – negative patient. Ind J Path Micro 2008; 51 (1): 74-5.
50. Adil A, Chikhaoui N, Ousehal A, Kdini R, Splenic tuberculosis apropos of 12 cases. Ann Radiol (paris) 1995; 38 : 403 – 7.

51. Kapoor R, Jain AK, Chaturbedi U, Saha MM. Ultrasound detection of tuberculomas of the spleen. Clin Radiol 1991; 43: 128-9.
52. Mitelstaedt CA, Pertain CL. Ultrasound – pathologic classification of splenic abnormalities – gray scale patterns. Radiology 1980; 134: 697 – 702.
53. Townsend RR, Laing FC, Jeffrey RB, et al. Abdominal lymphoma in AIDS evaluation with ultrasound. Radiology 1989. 171: 719-24.
54. Murray AW, Macgregor AB. A case of multiple splenic abscesses managed non-operatively. JR Coll Surg. Edinb 2000; 45: 189-91.
55. Gastrointestinal function and structure in HIV-positive patients. Lloyd R. Sutherland, MD, FRCPC; Deirdre L. Church, MD, FRCPC; Michael J. Gill, MD, FRCPC; James K. Kelly, MD, FRCPC; Wei-Sek Hwang, MD, FRCPC; Heather E. Bryant, MD, FRCPC
56. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded

surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep. 1992 Dec 18; 41 (RR – 17): 1-19.

57. Centers for Disease Control and Prevention. Guidelines for national human immunodeficiency virus case surveillance, including monitoring for human immunodeficiency virus infection and acquired immunodeficiency syndrome. MMWR Recomm Rep. 1999 Dec 10;48 (RR – 13) : 1-27, 29-31.
58. WHO Staging System for HIV infection and Disease in Adolescents and Adults, Table 3; Clinical Overview of HIV Disease. Accessed March 23, 2006.
59. World Health Organization. WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV – Related Disease In Adults and Children. 2007. Accessed March 30, 2009.
60. Increasing Mortality Due to End Stage Liver Disease in Patients with HIV Infection. Ioana Bica, Borbara McGovern, Division of Geographic Medicine and Infectious Disease, New England Medical Center, Boston.

61. Development of fatal acute liver failure in HIV-HBV coinfecting patients. Albert M Anderson, Marina B Mosunjac, World Journal of Gastroenterology.
62. Gastrointestinal Complications of HIV Disease HEPP REPORT. Joseph Bick, MD, Chief Medical Officer, California Medical Facility, California Department of Corrections.
63. Clinical profile of patients having splenic involvement in tuberculosis, Indian Journal of Tuberculosis. Ramakant Dixit, J.L.N.Medical College and Associated Group of Hospitals, Ajmer, Rajasthan.
64. Estimating the time period between infection and diagnosis based on CD4+ counts at first diagnosis among HIV-1 anti retroviral naive patients in Nigeria, Joseph C.Forbi, Thanda D.Forbi, Simon M. Agwale.
67. Dental and oral lesions in HIV infected patients: a study in Brazil. A Pinheiro, W Marcenes, JM Zakrzewska, PG Robinson
68. Connolly GM, Shanson D, Hawkins DA et al: Non-cryptosporidial diarrhoea in human immunodeficiency virus (HIV) infected patients. Gut 1989; 30: 195-200

69. Epidemiological study of Cryptosporidium infection among HIV/AIDS patients in Thailand. Srisuphanunt M, Suvedyathavorn V, Suputtamongkol Y, Arnantapunpong S, Viwatwongkasem C, Satitvipawee P; International Conference on AIDS (15th : 2004 : Bangkok, Thailand).
70. Cryptosporidiosis in HIV-seropositive Patients C Blanshard, Am Jackson, Dc Shanson, N Francis, Bg Gazzard
71. Management of ESLD in HIV Coinfection José M. Miró, Fernando Agüero, Montserrat Laguno, Christian Manzardo, Montserrat Tuset, Carlos Cervera, Asuncion Moreno, Juan-Carlos García-Valdecasas, Antonio Rimola, Hospital Clinic OLT in HIV Working Group.
72. Role of upper endoscopy in diagnosing opportunistic infections in human immunodeficiency virus infected patients. Ana Luiza Wernock – Silva, Ivete Bedin Prado. Casa da AIDS – Infectious Disease Division, School of Medicine, University of Sao Paulo, Sao Paulo, Brazil.

ANNEXURES

PROFORMA

GIT INVOLVEMENT IN NEWLY DIAGNOSED HIV PATIENTS

Name :

Age :

Sex :

OP/IP Number :

Address :

Ph.No :

New/Old patient :

CD4+ count :

PRESENTING COMPLAINTS :

SYSTEM INVOLVED :

GIT COMPLAINTS :

- 1.Dysphagia
- 2.Odynophagia
- 3.Abdominal pain
- 4.Abdominal distension&fullness
- 5.Jaundice
- 6.Diarrhea
- 7.Painful defecation
- 8.Anasarca

PAST HISTORY :

- 1.ART
- 2.ATT
- 3.SHT
- 4.PT
- 5.Psychiatric illness
- 6.DM

PERSONAL HISTORY :

- 1.Smoking
- 2.Alcoholism
- 3.IV Drug User
- 4.Mode of sexual contact

EXAMINATION :

Pallor :

Jaundice :

Lymphadenopathy :

Cyanosis :

Clubbing :

Pedal edema :

Vital Signs : BP- PR- Temp- RR-

CVS :

RS :

Abdomen :

CNS :

Genitalia :

Per rectal/Per vaginal examination(in females) :

INVESTIGATIONS :

CBC : HB% : TC : P : L : E : B : M :

Platelets :

LFT : TB : DB : SGOT/SGPT : ALP :

Total Protein/Albumin

HBsAg & Anti HCV: Stool Analysis :

USG Abdomen&Pelvis : OGD Scopy:

PATIENT CONSENT FORM

Gastro intestinal involvement in newly diagnosed HIV patients

Study centre : Govt.General hospital, MMC, Chennai

Patient's name :

Patient's age :

Identification number :

I confirm that I have understood the purpose of the procedures of the above study. I have had the opportunity to ask questions and all my questions have been answered satisfactorily.

☐

I understand that my participation in the study is entirely voluntary and that I am free to withdraw from the study at any time without my legal rights being affected

☐

I understand that sponsors of the study, others working on sponsor's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records both in respect of current study and any future research that may be conducted in relation to it; even if I withdraw from the study I agree to this access. However I understand that my identity will not be revealed in any information released to third parties unless required by law. I agree not to restrict the use of any data or results arising from the study.

☐

I agree to take part in the above the study and to comply with the instructions given during the study and inform about any change in my health status to the investigator.

☐

I hereby give permission to undergo complete clinical examination and investigations as part of the study.

☐

Signature of the patient

Patient's name and address place date

Signature of the investigator

Investigator's name place date

MASTER CHART

MASTER CHART																	
S. NO	NAME	AGE	SEX	NEW / OLD	CD4 CO	SYSTEM	DIAG	WHO CL	WHO IMM	CDC	GIT	STOOL	TBDB ALP OT/PT	ANTHCV/ HBSAG	USG	OGD	SPECIAL POINTS
1	JAYA	27	F	O	156	ABD	ESO CAN&ORAL THRUSH				DYS & ODYNOPHAGIA	NOT DONE	0.70.4 86 30/32	6.9/3.2 NEG	NORMAL	CONFLUENT YELLOWISH WHITE PLAQUES THAT OVERLIE AN ERETHEMATOUS MUCOSA	
2	RAVI	45	M	N	161	LYMPH	EXTRA PULMONARY TB	4	SEV	C3	NIL	NOT DONE	0.80.0 97 28/28	6.9/4.0 NEG	NORMAL	NOT DONE	MSM/EXTRAMARITAL
3	SUBBU VAIYAPUR	42	M	N	170	GIT	CRYPTOSPORIDIOSIS	4	SEV	C3	DIARRHEA	CRYPTOSPORIDIUM OOCYST+	0.70.5 76 32/30	6.5/3.9 NEG	NORMAL	NOT DONE	SHT-1 YEAR
4		40	F	N	382	ERM	PGL&HERPES ZOSTER	2	MIL	B2	LOWER ABDOMINAL PAIN	OVA&CYST NEG	0.80.5 86 32/22	6.3/4.0 NEG	NORMAL	CONFLUENT YELLOWISH WHITE PLAQUES THAT OVERLIE AN ERETHEMATOUS MUCOSA	
5	KADHAR BASHA	31	M	N	169	IT	ESO CAN&ORAL THRUSH	4	SEV	C3	DYS & ODYNOPHAGIA	NOT DONE	0.90.6 97 33/22	6.1/3.5 NEG	NORMAL		
6	DHANARA M	39	M	O	116	GIT	ABD TUBERCULOSIS				ABDOMINAL PAIN&DISTENSION	NOT DONE	1.00.8 72 42/41	6.8/3.9 NEG	MULTIPLE HYPO ECHOIC FOCI SEEN THROUGHOUT SPLEEN/ASCITES/PERI PORTAL NODES		A/F ADA ELEVATED EXUDATE WITH PREDOMINANT LYMPHOCYTES
7	SELVI	35	F	O	402	NIL	NIL				NIL	NOT DONE	1.10.7 85 32/24	6.5/3.2 NEG	NORMAL	NOT DONE	
8	NAGAMAN I	32	F	N	176	GIT	CRYPTOSPORIDIOSIS	4	SEV	C3	DIARRHEA	CRYPTOSPORIDIUM OOCYST+	1.10.7 96 45/36	5.6/3.0 NEG	THICKENED GALL BLADDER WALL 8MM.	NOT DONE	
9	BALAN	40	M	O	134	RS/GIT	DISSEMINATED TB				ABDOMINAL FULLNESS&DIARRHEA	OVA&CYST NEG	0.80.6 86 43/35	5.2/2.9 NEG	RIGHT PLEURAL EFFUSION/ASCITES LOCULATED WITH SEPTATIONS/MULTIPLE HYPO ECHOIC LESIONS IN SPLEEN	NOT DONE	PIF ADA ELEVATED EXUDATE WITH PREDOMINANT LYMPHOCYTES/AFB CULTURE POSITIVE
10	RAMESH	50	M	O	72	RS/ABD	DISSEMINATED TB				ABDOMINAL FULLNESS&DIARRHEA	OVA&CYST NEG	0.90.7 98 32/23	4.6/2.3 NEG	RIGHT PLEURAL EFFUSION/CELL&RETROCAVAL LYMPHADENOPATHY/MULTIPLE HYPO ECHOIC LESIONS IN SPLEEN	NOT DONE	SPUTUM AFB SMEAR POSITIVE/PIF ADA ELEVATED EXUDATE WITH PREDOMINANT LYMPHOCYTES
11	ELANGOV AN	45	M	N	129	M	HERPES ZOSTER	3	SEV	B3	DIARRHEA	OVA&CYST NEG	1.00.8 76 32/34	5.9/3.8 NEG	NORMAL	NOT DONE	HIO PSYCHIATRIC DISORDER FOR 5 YEARS
12	GANESAN	34	M	N	195	IT	DISSEMINATED CANDIDIASIS	4	SEV	C3	DYS & ODYNOPHAGIA	NOT DONE	0.80.6 65 30/34	5.3/2.3 NEG	PARA AORTIC LYMPHADENOPATHY/ GASTRIC WALL THICKENING /MULTIPLE HYPO ECHOIC LESIONS IN SPLEEN	ORAL THRUSH/CONFLUENT YELLOWISH WHITE PLAQUES THAT OVERLIE AN ERETHEMATOUS MUCOSA	
13	PARIMAL ALAGAN KAMATCHI	50	M	N	39	GIT	CRYPTOSPORIDIOSIS	4	SEV	C3	DIARRHEA	CRYPTOSPORIDIUM OOCYST+	0.90.6 75 32/34	6.0/3.0 NEG	NORMAL	NOT DONE	
14		29	F	N	273	CNS	AIDP		ADV	B2	NIL	NOT DONE	1.10.8 65 40/44	7.0/3.5 NEG	NORMAL	NOT DONE	
15	ADAKKAN	33	M	N	128	CNS	AIDP		SEV	B3	NIL	NOT DONE	0.80.6 65 32/24	5.5/3.2 NEG	NORMAL	NOT DONE	CSF & CNS
16	MANI	44	M	N	126	GENITAL	HSV 2 INFECTION	4	SEV	C3	NIL	NOT DONE	0.90.7 56 40/44	6.5/3.2 NEG	NORMAL	NOT DONE	TZANCK SMEAR POSITIVE
17	LAKSHMI	40	F	N	176	/GIT	ORAL THRUSH	3	SEV	B3	NIL	NOT DONE	1.30.9 59 48/51	7.0/3.5 NEG	NORMAL	NOT DONE	
18	RAJA PAPPAM	27	M	N	93	GIT	CRYPTOSPORIDIOSIS&A CALCULOUS CHOLECYSTITIS	4	SEV	C3	ABD PAIN&DIARRHEA	CRYPTOSPORIDIUM OOCYST+	2.1/1.6 119 51/34	5.3/2.3 NEG	GALLBLADDER ENLARGED WITH A THICK WALL (14 MM) /PERICHOLECYSTIC FLUID		CT ABDOMEN
19	MURUGA	35	F	N	218	FEVER	NIL	3	ADV	B2	NIL	NOT DONE	0.90.7 56 32/24	6.5/3.2 NEG	NORMAL	NOT DONE	
20		35	M	N	118	SPINE	SPINAL TB	4	SEV	C3	NIL	NOT DONE	0.80.6 94 22/17	5.2/2.1 NEG	NORMAL	NOT DONE	MRI WHOLE SPINE

(41)

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-600 003

Telephone 25363970
Fax 044 2535115
Dated : 12.05.2010

L.Dis.No.14597/ME5/Ethics Dean/MMC/2010

Title of the work : "Gastro Intestinal involvement in newly diagnosed HIV Patients"

Principal Investigator : Dr. A. Sangeetha.
Designation : PG in MD General Medicine
Department :


Madrass Medical College & G.G.H, Ch-3.

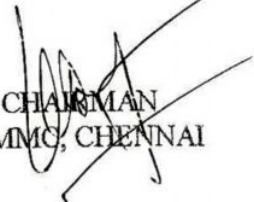
The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 12th May 2010 at 2.p.m in Pharmacology Seminar Hall, Madras Medical College, Chennai -3

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
4. You should not deviate from the area of the work for which you applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulation of the institution(s).
7. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.


SECRETARY
IEC, MMC, CHENNAI


CHAIRMAN
IEC, MMC, CHENNAI


DEAN
MADRAS MEDICAL COLLEGE,
CHENNAI